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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,964	10/13/2005	Hiroshi Terada	80253(302741)	3134

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EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
05/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,964	TERADA ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12,13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 12-13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 3/3/2009 and 4/2/2009 have been entered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 13 recites "being a fine particle formulation wherein diameters of great mass of the particle formulations are 1 and 6 microns".

Applicant states that this is supported in Figure 2 of the instant specification, which shows that diameters, of around 90% of the particle formulations, are 1 to 6 microns. However, the concept of connecting the range "1 to 6 microns" to particles of a certain mass was not disclosed in the specification or in the original claims.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites "PEG (polyethyleneglycol)" and further recites "PEO (polyethylene oxide)". These two names are synonyms for the same compound, $-(CH_2CH_2O)_n-$. It is unclear how one could choose between identical elements. This leaves uncertainty as to whether these terms are being used in their normal, accepted sense, or if one (or both) of the terms mean something other than the compound $-(CH_2CH_2O)_n$. For example, do one (or both) of these terms encompass structures where the compound $-(CH_2CH_2O)_n-$ is further bound to another compound (such as a PEGylated protein or polyoxyethylated castor oil)? Claim 13 recites the same names and is indefinite for the same reason.

Claim 13 further recites "being a fine particle formulation wherein diameters of great mass of the particle formulations are 1 and 6 microns". This phrase renders the claim indefinite for the following reasons:

(1) The phrase could be interpreted that the diameters have mass ("wherein diameters of great mass"). Diameter is a measurement of length, and has no mass.

(2) If the phrase is interpreted that particles of great mass have diameters ranging from 1 to 6 microns, then it is unclear what value is to be used to determine which particles have great mass (i.e. a certain minimum weight value, a certain minimum weight percentage, etc).

(3) The term "great mass" is a relative term. It is unclear what ranges constitute "great" (i.e. greater than 2 micrograms, greater than 20 micrograms, greater than 80 wt%, greater than 99 wt%, etc). The term "great mass" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(4) It is unclear if the components disclosed in claim 13 are separate particles from those disclosed in claim 1, or are instead an additional component (such as another coating layer) of the particles of claim 1. Accordingly, it is unclear if the diameter range "1 to 6 microns" applies to the components disclosed in claim 13 (in particle form), or to the particles of claim 1 when the particles further comprise the components of claim 13. This is further complicated by the recitation of "particle formulations" (plural) in claim 13, which opens another interpretation that the particles of

claim 1 and the components of claim 13 (in particle form) are combined (particle formulations), which together have diameters of 1 to 6 microns.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 12-13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20020106461 ('461) in view of US 5759583 ('583). '461 discloses a formulation comprising particles of rifampicin coated with a polymer coating selected from polymers including PLGA and polyethylene glycol, and mixtures thereof (see paragraphs 55, 64, 102, 139). The particles are prepared by physical vapor deposition of the coating onto the rifampicin core (see paragraph 55). The deposited PLGA has a molecular weight of 7,000 daltons (see paragraphs 36). The particle diameters may range from 0.1 microns to 2-3 mm (see paragraph 107). '461 fails to teach PLGA with a lactic acid to glycolic acid ratio range of 50:50 to 75:25 (instant claim 1). '461 further fails to teach fabrication of the particle formulation by membrane emulsification (instant claim 16).

'583 teaches that PLGA with a lactic acid to glycolic acid ratio range of 50:50 and a molecular weight of 10,000 is known in the art as a non-toxic biodegradable matrix for long-acting drug delivery of pharmaceutical agents (see col 1, lines 6-49; col 3, lines 18-25). The polymer provides these advantages regardless of matrix geometry (see col 2, lines 50-55).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to incorporate the PLGA taught by '583 into the formulation of '461, to improve the efficacy of the formulation. The rationale for this is that the PLGA of '583 is a non-toxic biodegradable matrix that provides long-acting drug delivery of pharmaceutical agents. Thus, it would be reasonable to try the PLGA of '583 in the formulation of '461 thereby incorporating the advantages of '583 into '461. The

expectation of success is high, as (1) '583 already contemplates similar molecular weight PLGA (7,000) and (2) the art recognizes that a lactic acid to glycolic acid ratio of 50:50 and a molecular weight of 10,000 provides a non-toxic biodegradable matrix with long-acting drug delivery.

Regarding the range 1 to 6 microns, it is the position of the Examiner that, as "great mass" is indefinite (see ***Claim Rejections - 35 USC § 112, Second Paragraph*** above), reasonably some mass of the particles ranging from 0.1 microns to 2-3 mm of '461 have particle diameters of 1 to 6 microns. In the alternative, it would have been obvious to optimize the particle diameter of the formulation to improve the efficacy of the formulation. In this way, one would find the instantly claimed range of 1 to 6 microns, which falls entirely within the broader range of 0.1 microns to 2-3 mm taught by '461. See MPEP § 2144.05, II.

Regarding the limitation "with phagocytic activity of macrophages being facilitated by the incorporation into macrophages of a particle formulation of PLGA [poly(lactic acid/glycolic acid)] copolymer] containing a medicament... and all or part of the pathogens present in the macrophages are exterminated to vanish", the Examiner is interpreting the "remedy" to be a composition of matter, and the above phrase to be an intended use of the composition. The recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the present case, the particle formulation that is rendered obvious by '461 in view of

'583 meets all the structural limitations of the instant claims, and must be capable of performing the intended use.

Instant claim 16 is directed to a product-by-process. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP § 2113. In the instant case, the method of making taught by '461 would produce the same particle formulation as the method disclosed in instant claim 16.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric E Silverman/
Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

May 1, 2009